

Comparison of Different Doses of Dexmedetomidine in Attenuating Extubation Response in Patients with Hypertension Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Objective: To compare different doses of dexmedetomidine in attenuating extubation response in hypertensive patients undergoing laparoscopic cholecystectomy.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Anesthesia, Combined Military Hospital, Rawalpindi Pakistan, from Sep 2022 to Feb 2023.

Methodology: Patients were segregated into two groups D1 (n=90) and D2 (n=90). Group-D1 received 0.5 mcg/kg of Dexmedetomidine in 10 ml of normal saline while Group-D2 received 1 mcg/kg of Dexmedetomidine diluted in normal saline (10 ml). Both the titrations were administered as an infusion over 10 minutes before extubation.

Results: Post-extubation mean heart rate varied from 86.27 ± 3.48 beats per minute in the D1 versus 66.01 ± 1.69 beats per minute in the Group-D2 ($p < 0.001$). Similarly, mean arterial pressure varied from 97.40 ± 1.23 mmHg in D1 to 80.88 ± 1.77 mmHg in the Group-D2 ($p < 0.001$). The quality of extubation was statistically better in the Group-D2 ($p < 0.001$).

Conclusion: We conclude that 1 mcg/kg of Dexmedetomidine is a better dose than 0.5 mcg/kg in blunting extubation responses and providing more than satisfactory control of bradycardia and hypotension which is advantageous during extubation.

Keywords: Cholecystectomy, Dexmedetomidine, Extubation, Hypertensive, Laparoscopic.

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INTRODUCTION

The process of extubation remains a challenge for the anesthetist. It is said that that extubation is an art which requires careful planning, precise execution, and constant monitoring for smooth recovery of the patient.¹ Extubation if not done carefully is associated with various complications including hypertension, laryngospasm, bronchospasm, pulmonary edema, persistent cough, and airway edema.² All these complications are associated with the technique and procedure of the extubation resulting in release of catecholamines and the sympathetic response encountered once the patient returns from the planes of general anesthesia and muscle paralysis.³

The complications associated with the extubation response discussed above are more profound and severe with patients with co-morbidities or nature of surgery associated with hemodynamic compromise resulting in more care needed to successfully extubate the patient.⁴ The co-morbidities include diabetes,

hypertension, ischemic heart disease, chronic kidney and liver disease and surgeries include major intra-abdominal surgeries and those associated with poor lung compliance like insufflation of carbon dioxide in laparoscopic surgeries.⁵

Dexmedetomidine belongs to the class of alpha-2 agonists and has been introduced as an effective agent for various medical indications including ICU sedation,⁶ adjunct to pre-operative medications as an anxiolytic and to blunt response to sympathetic response in patients. This makes it a very appropriate agent to blunt the response to intubation as well.⁷

International literature supports its use as an adjunct to blunt extubation responses in patients. However, data is lacking regarding the use of the appropriate dose to be used resulting in minimum side effect profile in patients with co-morbidities like hypertension where increasing doses maybe needed to blunt the response.

The objective of this study was to compare different doses of Dexmedetomidine for blunting response to intubation in hypertensive patients and checking the quality achieved by each dose administered.

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METHODOLOGY

This quasi-experimental study was carried out at the Anesthesia Department, Combined Military Hospital, Rawalpindi Pakistan from Sep 2022 to Feb 2023 after approval from the ethical review board (vide letter no. 374). With a 5% level of significance, 80% test power, minimum sample size was calculated by WHO calculator with mean difference in heart rate in both groups from the baseline being 15.10 ± 5.63 and 13.34 ± 6.24 beats per minute respectively. Minimum sample size for each group came out to be 69 and 89 patients respectively.⁸ Keeping this as reference, we analyzed 260 patients, and a total of 180 patients were then included in the study protocol with 90 in each group marked as Group-D1 and Group-D2. Sampling technique employed was non-probability, consecutive sampling and we randomized the study sample into two sets by sealed envelope. Until the time of surgery, the anaesthesiologist and participants were both unaware of the randomization sequence (Figure).

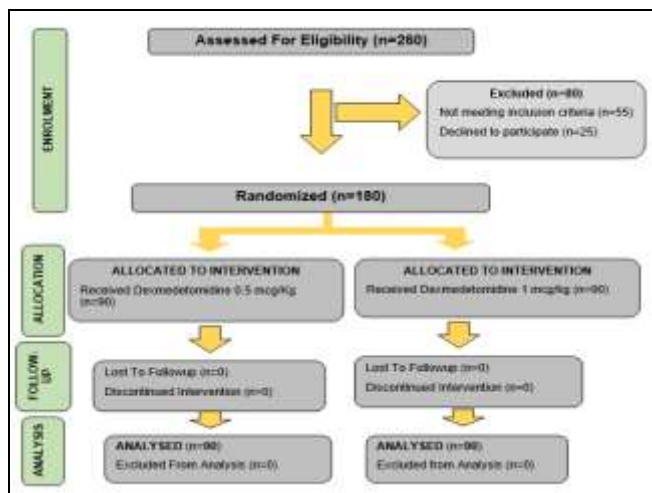


Figure: Phases of the Study

Inclusion Criteria: ASA-II male and female patients with controlled and treated hypertension between ages 45-55 years, with a BMI (body mass index) of 20-25 kg/m² presenting in the anesthesia department for elective laparoscopic cholecystectomy for cholelithiasis were included.

Exclusion Criteria: Patients with metastatic disease, major cardiac or respiratory disease, low ejection fraction, post chemotherapy, indications for cholecystectomy other than cholelithiasis, patients developing adverse effects with Dexmedetomidine (Mean Arterial Pressure <60 or heart rate <50) and unwilling to be included in the study were excluded.

The study method included all patients as per the inclusion criteria furnished. The method of sampling was non-probability consecutive sampling according to the inclusion criteria above. Patients were divided into two groups, Group-D1 (n=90) and Group-D2 (n=90). Group-D1 received 0.5 mcg/kg of Dexmedetomidine in 10 ml of normal saline while Group-D2 received 1 mcg/kg of Dexmedetomidine in 10 ml of normal saline. Both the titrations were administered as an infusion before extubating the patient over 10 minutes. This was a double-blind study with the anesthetist in the OT receiving a sealed envelope with the instructions for the infusion and drug preparation in both the groups. Findings were written on a proforma by a resident anesthetist in the OT unaware of the drug or the study protocol.

Nil per oral status was checked and confirmed at the day of surgery in the recovery room, patients were taken to the OT. Monitoring was attached to all participants which included non-invasive blood pressure, heart rate, capnography and ECG were attached to participants in both groups. Pre-operative blood pressure was checked in all participants and MAP (mean arterial pressure) was recorded. Anesthesia was then induced in both groups with IV Propofol 2 mg/kg, IV Atracurium 0.5 mg/kg with maintenance dose with 50% oxygen with Isoflurane at 1.0 Minimum Alveolar Concentration. Patients were kept in the 15-20-degree Trendelenburg position with ventilation maintained at 6-8 ml/kg and respiratory rate at 14-16 breaths/min in both the groups maintaining an end-tidal carbon dioxide concentration between 35-45 mmHg. The abdomen was then insufflated with carbon dioxide with intra-abdominal pressure maintained at 12 mm Hg. At the end of surgery, the carbon dioxide was flushed out of the abdominal cavity. At the end of the procedure, Isoflurane was discontinued at the end of abdominal closure and infusion of Dexmedetomidine was started in both the groups with the assigned drug doses when the TOF ratio (train of four) for monitoring of neuromuscular recovery reached >0.7. Patients were then extubated after 10 minutes or when TOF ratio was >0.9. Neostigmine 0.05 mg/kg and Glycopyrrolate 0.01 mg/kg were given for reversal of muscle paralysis.

Primary variable measured was quality of extubation using a 5-point standardized scale evaluation based on: 1 = no coughing, 2 = smooth extubation, minimal coughing (1 or 2 times), 3 =

moderate coughing (3 or 4 times), 4 = severe coughing (5-10 times) and straining, 5 = poor extubation, very uncomfortable (laryngospasm and coughing >10 times).⁹ Secondary variables measured were heart rate, mean arterial pressure and spO_2 immediately following extubation. Demographic data were statistically described in terms of mean and SD. Chi-square test was used to see statistical difference between both groups for quality of extubation. Independent Samples t-test was used to evaluate mean values for heart rate, mean arterial pressure and saturation of peripheral oxygen (spo_2). A p -value of ≤ 0.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for Social Sciences 26.0.

RESULTS

A total of 180 patients were included in the study divided into the D1 ($n=90$) and D2 ($n=90$) groups. Mean age of patients was 48.77 ± 3.06 years in the D1 versus 48.58 ± 2.99 years in the D2 group ($p=0.07$). Mean BMI was 22.77 ± 1.10 kg/m^2 in the D1 versus 22.67 ± 1.10 kg/m^2 in the D2 group ($p=0.14$). The duration of surgery was 68.36 ± 3.70 minutes in the D1 versus 68.19 ± 3.70 minutes in the D2 group ($p=0.07$). Gender distribution showed 37(41.1%) males versus 53(58.9%) females in the D1 group versus 43(47.8%) males versus 47(52.2%) females in the D2 group. (Table-I).

Table-I: Comparison of Demographic and Physiological Parameters Between Both Groups ($n=180$)

Variable(s)	Group-D1 ($n=90$)	Group-D2 ($n=90$)	p -value
Mean Age (Years)	48.77 ± 3.06	48.58 ± 2.99	0.078
Mean BMI (Kg/ m^2)	22.77 ± 1.10	22.67 ± 1.10	0.140
Mean Duration of Surgery (Min)	68.36 ± 3.71	68.19 ± 3.70	0.079
Mean Heart Rate (Beats Per Minute)	86.27 ± 3.48	66.01 ± 1.69	<0.001
Mean Arterial Pressure (Mm Hg)	97.40 ± 1.23	80.88 ± 1.77	<0.001
Mean Oxygen Saturation (%)	97.88 ± 0.63	97.92 ± 0.56	0.158
Gender ($n\%$)			
Male	37(41.1%)	43(47.8%)	-
Female	53(58.9%)	47(52.2%)	

The vital parameters immediately post-extubation, mean heart rate varied from 86.27 ± 3.48 beats per minute in the D1 versus 66.01 ± 1.69 beats per minute in the D2 group ($p<0.001$). Similarly, mean arterial pressure varied from 97.40 ± 1.23 mmHg in D1 to 80.88 ± 1.77 mmHg in the D2 group ($p<0.001$). The values of oxygen saturation were comparable between both groups with 97.88 ± 0.63 percent in the D1 versus 97.92 ± 0.56 percent in the D2 group ($p=0.158$) (Table-I).

The primary outcome assessing quality of extubation showed, patients in the D1 group had 23(25.6%) patients achieving a numeric score 1, 36(40%) patients scoring 2, 24(26.7%) patients scoring 3 while 07(7.8%) patients scoring 4 on the standard numerical scale. In comparison, patients in group D2 achieved an extubation quality score of 1 in 59(65.6%) cases, 2 in 20(22.2%) of the cases and 11(12.2%) cases achieving a score of 3 while extubating. The quality of extubation was statistically better in the D2 group ($p<0.001$) (Table-II).

Table-II: Comparison of Quality of Extubation Among Groups ($n=180$)

Quality of Extubation (Numeric Score 1-5)	Group-D1 ($n=90$) $n(\%)$	Group-D2 ($n=90$) $n(\%)$	p -value
1	23(25.6%)	59(65.6%)	<0.001
2	36(40.0%)	20(22.2%)	
3	24(26.7%)	11(12.2%)	
4	07(7.8%)	00(0.0%)	
5	00(0.0%)	00(0.0%)	

5-point standardized scale evaluation for quality of extubation⁹

DISCUSSION

The findings of our study concluded that a dose of 1 mcg/kg provided better extubation conditions faring better on the extubation scale with patients more comfortable and less agitated while at the same time, the side effects of bradycardia and hypotension were in the acceptable range to be employed to all patients. The study was carried out at a tertiary care hospital receiving a significant patient clientele requiring laparoscopic cholecystectomy. The purpose of this study was to evaluate the role of Dexmedetomidine in attenuating physical responses to extubation; specifically in patients with hypertension on treatment where sympathetic drive and responses are more exaggerated during extubation which may result in considerable morbidity due to increased chances of complications¹⁰ which may be associated with laryngospasm, bronchospasm, airway edema, patient agitation, hypertensive emergency amongst others.¹¹

Dexmedetomidine is an alpha 2 agonist¹² that has found widespread acceptance especially in the ICU setups for its sedative, hypnotic and analgesic effects. Its sedative and hypnotic effects are attributable to its central action on the nervous system by inhibiting central sympathetic excitation whereas its analgesic effects are linked to its action on the spinal cord in the peripheral nervous system.¹³ These desirable effects can be employed in the operating room to provide good quality and effective extubation in patients where extubation is complex or tricky due to patient

co-morbidities.^{14,15} The only limitation to the drug is the dose dependent effect on heart rate and blood pressure resulting in bradycardia and hypotension which is preferable in the extubation scenario due to sympathetic overdrive once the patient comes back from the deeper planes of general anesthesia.¹⁶ However, where these clinical manifestations maybe desirable, we aimed to compare different doses and tried to achieve a balance between good quality smooth extubation and preventing profound bradycardia and hypotension.

The findings of our study concluded that a dose of 1 mcg/kg provided better extubation conditions faring better on the extubation scale with patients more comfortable and less agitated while at the same time, the side effects of bradycardia and hypotension were in the acceptable range to be employed to all patients. None of the patients in the study showed serious adverse effects requiring pressor support or fluid boluses. This may also be attributable to the drug being administered as an infusion over time than bolus and this is recommended to achieve best results.¹⁷

Studies carried out for attenuating extubation response with Dexmedetomidine were consistent with the results of our study. When used in smokers with hyperactive airways prone to airway complications in a study,¹⁸ it resulted in better extubation quality and less incidence of complications when compared to control. Similarly, it was very effective in cough suppression during extubation in a study carried out by Jafarzadeh *et al.*¹⁹ Local studies also support its use in better tube toleration, good extubation times and better patient outcome.²⁰

RECOMMEDATIONS

The study recommends the use of Dexmedetomidine as an excellent agent in blunting extubation sympathetic responses resulting in better and smooth extubation.

LIMITATION OF STUDY

The limitations are that the study is single center only. A multi-center study would result in a wider demographic area with more confirmative results.

CONCLUSION

We conclude that 1 mcg/kg of Dexmedetomidine is a better dose than 0.5 mcg/kg in blunting extubation responses and providing more than satisfactory control of bradycardia and hypotension which is advantageous during extubation.

Conflict of Interest: None.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

OAM & MHS: Data acquisition, data analysis, critical review, approval of the final version to be published.

MHB & TAK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MI & JZ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Comparison of Dexmedetomidine

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